Applicants: James Binley et al.
Serial No.: 10/780,993
Filed: January 18, 2004
Exhibit 6

Office Action Summary	Application No.	Applicant(s)	
	10/489,040	MOORE ET AL.	
	Examiner	Art Unit	
	Louise Wang	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,20,21 and 32-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-16, 20-21,and 32-56* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Applicant's Preliminary Amendment, filed March 05, 2004, is acknowledged.

Claims 17-19, 22-31, and 57-111 have been canceled.

Claims 1-16, 20-21, and 32-56 are pending.

It is noted that claim 56 depends from a canceled claim. For examination purposes, claim 56 is treated as if it depends from claim 16. Clarification is required.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-4, 14, 15, in part, and 9, drawn to a stable HIV-1 pre-fusion envelope glycoprotein trimeric complex, wherein (i) each monomeric unit of the complex comprises HIV-1 gp120 and HIV-I gp41 produced by cleavage at a mutated furin recognition site, (ii) the gp41 has an I559P mutation at position A in its N-terminal helix, and (iii) the gp120 and gp41 are bound to each other by at least one disulfide bond between a cysteine residue introduced by an A492C mutation into gp120 and a cysteine residue introduced by a T596C mutation into gp41; and a composition comprising a pharmaceutically acceptable particle and the trimeric complex.

Group II, claims 1-4, 14, 15, in part, and 10, drawn to a stable HIV-1 pre-fusion envelope glycoprotein trimeric complex, wherein (i) each monomeric unit of the complex comprises HIV-1 gp120 and HIV-I gp41 produced by cleavage at a mutated furin recognition site, (ii) the gp41 has an I559P mutation at position D in its N-terminal helix, and (iii) the gp120 and gp41 are bound to each other by at least one disulfide bond between a cysteine residue introduced by an A492C mutation into gp120 and a cysteine residue introduced by a T596C mutation into gp41; and a composition comprising a pharmaceutically acceptable particle and the trimeric complex.

Group III, claims 1-4, 14, 15, in part, and 11-13, drawn to a stable HIV-1 pre-fusion envelope glycoprotein trimeric complex, wherein (i) each monomeric unit of the complex comprises HIV-1

gp120 and HIV-I gp41 produced by cleavage at a mutated furin recognition site, (ii) the gp41 has a substitution of a glycine with a proline in its N-terminal helix, and (iii) the gp120 and gp4l are bound to each other by at least one disulfide bond between a cysteine residue introduced by an A492C mutation into gp120 and a cysteine residue introduced by a T596C mutation into gp41; and a composition comprising a pharmaceutically acceptable particle and the trimeric complex.

Group IV, claims 5-8, 14, 15, in part, and 9, drawn to a polypeptide comprising the amino acid sequence of HIV-I gp120 and HIV-l gp41 produced by cleavage at a mutated furin recognition site, wherein (i) the gp4l sequence has an I559P mutation at position A in its N- terminal helix, and (ii) the gp120 and gp4l are bound to each other by at least one disulfide bond between a cysteine residue introduced by an A492C mutation into gp120 and a cysteine residue introduced by a T596C mutation into gp41.

Group V, claims 5-8, 14, 15, in part, and 10, drawn to a polypeptide comprising the amino acid sequence of HIV-I gp120 and HIV-l gp41 produced by cleavage at a mutated furin recognition site, wherein (i) the gp4l sequence has an I559P mutation at position D in its N- terminal helix, and (ii) the gp120 and gp4l are bound to each other by at least one disulfide bond between a cysteine residue introduced by an A492C mutation into gp120 and a cysteine residue introduced by a T596C mutation into gp41.

Group VI, claims 5-8, 14, 15, in part, and 11-13, drawn to a polypeptide comprising the amino acid sequence of HIV-I gp120 and HIV-l gp41 produced by cleavage at a mutated furin recognition site, wherein (i) the gp4l sequence has a substitution of a glycine with a proline in its N- terminal helix, and (ii) the gp120 and gp4l are bound to each other by at least one disulfide bond between a cysteine residue introduced by an A492C mutation into gp120 and a cysteine residue introduced by a T596C mutation into gp41.

Group VII, claims 5, in part, and 32-36, drawn to a nucleic acid which encodes a polypeptide comprising the amino acid sequence of HIV-I gp120 and HIV-l gp41, a vector comprising the nucleic acid with furin sequence, and a host cell comprising the vector.

Group VIII, claim 37, drawn to a method for producing a polypeptide which comprises growing the host cell comprising the vector under conditions permitting production of the polypeptide and recovering the polypeptide so produced.

Group IX, claims 1, in part, 16, 20, 21, and 38-43, drawn to a composition comprising the HIV-1 pre-fusion envelope glycoprotein trimeric complex with a pharmaceutical particle to be affixed to, a cytokine, a chemokine, an adjuvant, and a pharmaceutically acceptable carrier.

Group X, claims 44, in part, and 45, drawn to a method for eliciting an immune response in a subject against HIV-l or an HIV-1 infected cell comprising administering to the subject a prophylactically or therapeutically effective amount of the trimeric complex or the pharmaceutical composition of the trimeric complex in a single dose.

Group XI, claims 44, in part, and 46, drawn to a method for eliciting an immune response in a subject against HIV-1 or an HIV-1 infected cell comprising administering to the subject a prophylactically or therapeutically effective amount of the trimeric complex or the pharmaceutical composition of the trimeric complex in multiple doses.

Group XII, claims 44, in part, and 47, drawn to a method for eliciting an immune response in a subject against HIV-1 or an HIV-1 infected cell comprising administering to the subject a prophylactically or therapeutically effective amount of the trimeric complex or the pharmaceutical composition of the trimeric complex as part of a heterologous primer-boost regimen.

Group XIII, claims 1, 16, in part, and 48, drawn to a vaccine which comprises a therapeutically effective amount of the trimeric complex.

Group XIV, claims 1, 16, in part, and 49, drawn to a vaccine which comprises a prophylactically effective amount of the trimeric complex.

Group XV, claims 1, 16, in part, 50 and 52, drawn to a method for preventing a subject from becoming infected with HIV-1 comprising administering to the subject a prophylactically effective amount of the trimeric complex or the composition of the trimeric complex, thereby preventing the subject from becoming infected with HIV-1.

Group XVI, claims 1, 16, in part, 51 and 53, drawn to a method for reducing the likelihood of a subject's becoming infected with HIV-1 comprising administering to the subject a prophylactically effective amount of the trimeric complex or the composition of trimeric complex.

Group XVII, claims 1, 16, in part, and 54, drawn to a method for preventing or delaying the onset of, or slowing the rate of progression of, an HIV-1- related disease in an HIV-1-infected subject which comprises administering to the subject a therapeutically effective amount of the trimeric complex or the composition of trimeric complex.

Group XVIII, claims 1, 16, in part, 55 and 56, drawn to a method for producing the composition of trimeric complex, comprising contacting a pharmaceutically acceptable particle with a stable HIV-1 pre-fusion envelope glycoprotein trimeric complex under conditions permitting the complex to become operably affixed to the particle, wherein (i) each monomeric unit of the complex comprises HIV-1 gp120 and HIV-1 gp41, (ii) the gp41 has one or more mutations in its N-terminal helix, and (iii) the gp120 and gp41 are bound to each other by at least one disulfide bond between a cysteine residue introduced into the gp120 and a cysteine residue introduced into the gp41.

The inventions listed as Groups I-XVIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the common technical feature in all groups is the composition of HIV-1 pre-fusion envelope glycoprotein trimeric complex. However, it is not an improvement over the prior art of Binley *et al.* (2000) listed in the Information Disclosure Statement filed on 13 December 2004.

Binley teaches a recombinant HIV-1 envelope glycoprotein complex stabilized by a disulfide bond between the gp120 and gp41 subunits as claimed (see entire document). The reference specifically suggests mimicking the trimeric virion-associated structure to improve immunogenicity.

Therefore, the technical feature is not a contribution over the art, thus, the claimed invention cannot be said to have unity of invention.

Species Election

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Irrespective of which Group is elected, Applicant is required to elect one trimeric complex with one mutation as exemplified by claim 14, with nucleic acid and amino acid sequences listed by SEQ ID NO;

If Group VII is elected, Applicant is required to select a vector as exemplified by claim 35 with a nucleic acid sequence listed by SEQ ID NO;

If Group IX is elected, Applicant is required to select a particle as exemplified by claim 20 with a specific composition as exemplified by claim 21, a cytokine as exemplified by claim 40, a chemokine as exemplified by claim 41, and an adjuvant as exemplified by claim 43.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Joint Inventorship

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Contact Information

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Wang whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

L. Wang
Aug. 29, 2005

JEFFREY STUCKER
PRIMARY EXAMINER

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10/489,040	12/13/2004	John P. Moore	2048/65845-D-US-PCT-US/JP	1441

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Please find below and/or attached an Office communication concerning this application or proceeding.